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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/063,592 | 05/03/2002 | Dan L. Eaton | P3230R1C001-168 | 4535 |

30313 7590 01/13/2005

KNOBBE, MARTENS, OLSON & BEAR, LLP
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IRVINE, CA 92614

| EXAMINER | |
|---|---|
| KAUFMAN, CLAIRE M | |
| **ART UNIT** | **PAPER NUMBER** |
| 1646 | |

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/063,592 | EATON ET AL. | |
| | Examiner | Art Unit | |
| | Claire M Kaufman | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *03 May 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 May 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/13/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Claim Rejections - 35 USC §§ 101/112*

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are drawn to an antibody which (specifically) binds the polypeptide of SEQ ID NO:82. The specification asserts a number of utilities for both the polypeptide and encoding polynucleotide, however, these utilities are not specific and substantial or well established. If the polypeptide antigen does not have utility, then the antibody which binds it does not have a specific and substantial utility. For example, in Example 10 (pages 132-133), it is asserted that the polypeptide may be used as an antigen to make antibodies. Because neither the physiological nor the clinical significance of the polypeptide is known, and because the prior art does not support a very close structural relationship to a well described family of known proteins by both structure and function, the polypeptide does not have utility as required by 35 USC 101. If one does not know what the protein to which the antibody binds does or what disease it is specifically associated with, then the antibody that binds the protein likewise does not have utility. The ability to isolate a protein, detect expression changes of the protein and diagnose disease by using an antibody is not a specific or substantial use if it is not known what the isolated or expressed protein does or what specific disease can by diagnosed with it.

Another possible utility comes for the finding that the encoding polynucleotide is "more highly expressed" in normal esophagus and kidney as compared to esophageal or kidney tumor tissue (Example 18, p. 142). There is no guidance on how to use this information. No levels (relative or absolute) are disclosed. This information is too sparse to allow the encoding polynucleotide to be used as a diagnostic marker for esophageal or kidney tumor. Further, even if the polynucleotide had utility as a tumor marker, the encoded polypeptide has no such utility since there is no reason to suspect that there is alteration of polypeptide sequence or amount in esophageal or kidney tumor *versus* normal tissue. It is not known what the protein does or if the level of the protein of SEQ ID NO:82 in esophageal or kidney tumors corresponds to nucleic acid transcript level, *i.e.*, if increased gene amplification in tumors corresponds to a increase in amount of expressed protein.

It is important to note that the instant specification provides no information regarding increased mRNA or protein levels of PRO1557 in tumor samples relative to normal samples. Only relative gene expression data was presented. It is noted that the literature cautions researchers from drawing conclusions based on small changes in transcript expression levels between normal and cancerous tissue. For example, Hu et al. (2003, Journal of Proteome Research 2:405-412) analyzed 2286 genes that showed a greater than 1-fold difference in mean expression level between breast cancer samples and normal samples in a micoarray (p. 408, middle of right column). Hu et al. discovered that, for genes displaying a 5-fold change or less in tumors compared to normal, there was no evidence of a correlation between altered gene expression and a known role in the disease. However, among genes with a 10-fold or more change in expression level, there was a strong and significant correlation between expression level and a published role in the disease (see discussion section). However, in the instant application it is not disclosed whether or not the polypeptide levels correlate with nucleic acid (either DNA or mRNA) levels. So one cannot base the use of the polypeptide or binding antibody on the expression of the nucleic acid.

For these reasons, there is no substantial and specific utility for the claimed antibody.

Claims 1-6 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well

established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

It would require significant further experimentation to be able to use the claimed antibody because no definite function or directly associated disease has been determined for the protein of SEQ ID NO:82. No function can be reasonably assigned to the polypeptide antigen based on its homology to another protein(s).

### *35 U.S.C. § 102*

The following rejections under 35 U.S.C. § 102 are made under the assumption that the effective filing date for the instantly claimed invention is 05/03/2002, which is the actual filing date of the instant application. Applicant is advised that the instant application can only receive benefit under 35 U.S.C. §120 from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, with respect to the new claimed invention. Because the instant application does *not* meet the requirements of 35 U.S.C. § 112, first paragraph, for the reasons given above and it is a continuing application of Serial Number 10/006,867, the prior application also does not meet those requirements for the claimed invention and, therefore, is unavailable under 35 U.S.C. § 120.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 200070049.

WO 200070049 teaches the protein of SEQ ID NO:13 which is 100% identical SEQ ID NO:82 of the instant application (see below comparison), as well as an antibody that specifically binds to the protein (*e.g.*,p. 62, line 24-p.63, line 4). These antibodies taught include

monoclonal, humanized, labeled and antibody fragments (p. 39, lines 30-through p. 40, line 19, p. 19, lines 27-29, p. 46, lines 13-15).

***Comparison of WO 200070049 to SEQ ID NO:81 and 82***

```
LOCUS       AX048199               1720 bp    DNA     linear   PAT 15-DEC-2000
DEFINITION  Sequence 39 from Patent WO0070049.
ACCESSION   AX048199
VERSION     AX048199.1  GI:11876989
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1
  AUTHORS   Tang,Y.T., Yue,H., Lal,P., Burford,N., Bandman,O., Baughn,M.R.,
            Azimzai,Y., Lu,D.A. and Patterson,C.
  TITLE     Extracellular signaling molecules
  JOURNAL   Patent: WO 0070049-A 39 23-NOV-2000;
            Incyte Genomics, Inc. (US)
FEATURES             Location/Qualifiers
     source          1. .1720
                     /organism="Homo sapiens"
                     /mol_type="unassigned DNA"
                     /db_xref="taxon:9606"
                     /note="Incyte ID No: 2267403CB1"
ORIGIN

  Query Match             99.3%;  Score 1720;  DB 6;  Length 1720;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 1720;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy=SEQ ID NO:81  1 CCCACGCGTCCGCGCCTCTCCCTTCTGCTGGACCTTCCTTCGTCTCTCCATCTCTCCCTC 60
                   ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db               1 CCCACGCGTCCGCGCCTCTCCCTTCTGCTGGACCTTCCTTCGTCTCTCCATCTCTCCCTC 60

Qy              61 CTTTCCCCGCGTTCTCTTTCCACCTTTCTCTTCTTCCCACCTTAGACCTCCCTTCCTGCC 120
                   ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db              61 CTTTCCCCGCGTTCTCTTTCCACCTTTCTCTTCTTCCCACCTTAGACCTCCCTTCCTGCC 120

Qy             121 CTCCTTTCCTGCCCACCGCTGCTTCCTGGCCCTTCTCCGACCCCGCTCTAGCAGCAGACC 180
                   ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db             121 CTCCTTTCCTGCCCACCGCTGCTTCCTGGCCCTTCTCCGACCCCGCTCTAGCAGCAGACC 180

Qy             181 TCCTGGGGTCTGTGGGTTGATCTGTGGCCCCTGTGCCTCCGTGTCCTTTTCGTCTCCCTT 240
                   ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db             181 TCCTGGGGTCTGTGGGTTGATCTGTGGCCCCTGTGCCTCCGTGTCCTTTTCGTCTCCCTT 240

Qy             241 CCTCCCGACTCCGCTCCCGGACCAGCGGCCTGACCCTGGGGAAAGGATGGTTCCCGAGGT 300
                   ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db             241 CCTCCCGACTCCGCTCCCGGACCAGCGGCCTGACCCTGGGGAAAGGATGGTTCCCGAGGT 300

Qy             301 GAGGGTCCTCTCCTCCTTGCTGGGACTCGCGCTGCTCTGGTTCCCCCTGGACTCCCACGC 360
                   ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db             301 GAGGGTCCTCTCCTCCTTGCTGGGACTCGCGCTGCTCTGGTTCCCCCTGGACTCCCACGC 360
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Qy        361 TCGAGCCCGCCCAGACATGTTCTGCCTTTTCCATGGGAAGAGATACTCCCCCGGCGAGAG 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy        421 CTGGCACCCCTACTTGGAGCCACAAGGCCTGATGTACTGCCTGCGCTGTACCTGCTCAGA 480
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Qy        481 GGGCGCCCATGTGAGTTGTTACCGCCTCCACTGTCCGCCTGTCCACTGCCCCCAGCCTGT 540
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Qy        541 GACGGAGCCACAGCAATGCTGTCCCAAGTGTGTGGAACCTCACACTCCCTCTGGACTCCG 600
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Db        541 GACGGAGCCACAGCAATGCTGTCCCAAGTGTGTGGAACCTCACACTCCCTCTGGACTCCG 600

Qy        601 GGCCCCACCAAAGTCCTGCCAGCACAACGGGACCATGTACCAACACGGAGAGATCTTCAG 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 GGCCCCACCAAAGTCCTGCCAGCACAACGGGACCATGTACCAACACGGAGAGATCTTCAG 660

Qy        661 TGCCCATGAGCTGTTCCCCTCCCGCCTGCCCAACCAGTGTGTCCTCTGCAGCTGCACAGA 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 TGCCCATGAGCTGTTCCCCTCCCGCCTGCCCAACCAGTGTGTCCTCTGCAGCTGCACAGA 720

Qy        721 GGGCCAGATCTACTGCGGCCTCACAACCTGCCCCGAACCAGGCTGCCCAGCACCCCTCCC 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 GGGCCAGATCTACTGCGGCCTCACAACCTGCCCCGAACCAGGCTGCCCAGCACCCCTCCC 780

Qy        781 ACTGCCAGACTCCTGCTGCCAAGCCTGCAAAGATGAGGCAAGTGAGCAATCGGATGAAGA 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 ACTGCCAGACTCCTGCTGCCAAGCCTGCAAAGATGAGGCAAGTGAGCAATCGGATGAAGA 840

Qy        841 GGACAGTGTGCAGTCGCTCCATGGGGTGAGACATCCTCAGGATCCATGTTCCAGTGATGC 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 GGACAGTGTGCAGTCGCTCCATGGGGTGAGACATCCTCAGGATCCATGTTCCAGTGATGC 900

Qy        901 TGGGAGAAAGAGAGGCCCGGGCACCCCAGCCCCCACTGGCCTCAGCGCCCCTCTGAGCTT 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 TGGGAGAAAGAGAGGCCCGGGCACCCCAGCCCCCACTGGCCTCAGCGCCCCTCTGAGCTT 960

Qy        961 CATCCCTCGCCACTTCAGACCCAAGGGAGCAGGCAGCACAACTGTCAAGATCGTCCTGAA 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 CATCCCTCGCCACTTCAGACCCAAGGGAGCAGGCAGCACAACTGTCAAGATCGTCCTGAA 1020

Qy       1021 GGAGAAACATAAGAAAGCCTGTGTGCATGGCGGGAAGACGTACTCCCACGGGGAGGTGTG 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 GGAGAAACATAAGAAAGCCTGTGTGCATGGCGGGAAGACGTACTCCCACGGGGAGGTGTG 1080

Qy       1081 GCACCCGGCCTTCCGTGCCTTCGGCCCCTTGCCCTGCATCCTATGCACCTGTGAGGATGG 1140
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Qy       1141 CCGCCAGGACTGCCAGCGTGTGACCTGTCCCACCGAGTACCCCTGCCGTCACCCCGAGAA 1200
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Qy       1201 AGTGGCTGGGAAGTGCTGCAAGATTTGCCCAGAGGACAAAGCAGACCCTGGCCACAGTGA 1260
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Qy       1261 GATCAGTTCTACCAGGTGTCCCAAGGCACCGGGCCGGGTCCTCGTCCACACATCGGTATC 1320
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Qy       1321 CCCAAGCCCAGACAACCTGCGTCGCTTTGCCCTGGAACACGAGGCCTCGGACTTGGTGGA 1380
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Qy       1381 GATCTACCTCTGGAAGCTGGTAAAAGATGAGGAAACTGAGGCTCAGAGAGGTGAAGTACC 1440
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy       1441 TGGCCCAAGGCCACACAGCCAGAATCTTCCACTTGACTCAGATCAAGAAAGTCAGGAAGC 1500
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Qy       1501 AAGACTTCCAGAAAGAGGCACAGCACTTCCGACTGCTCGCTGGCCCCCACGAAGGTCACT 1560
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Qy       1561 GGAACGTCTTCCTAGCCCAGACCCTGGAGCTGAAGGTCACGGCCAGTCCAGACAAAGTGA 1620
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             ||||||||||||||||||||||||||||||||||||||||
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Claim 1; Page 90-91; 114pp; English.

Query Match 100.0%; Score 2545; DB 4; Length 451;
Best Local Similarity 100.0%; Pred. No. 3.4e-172;
Matches 451; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy                61 CTCSEGAHVSCYRLHCPPVHCPQPVTEPQQCCPKCVEPHTPSGLRAPPKSCQHNGTMYQH 120
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Qy               181 QSDEEDSVQSLHGVRHPQDPCSSDAGRKRGPGTPAPTGLSAPLSFIPRHFRPKGAGSTTV 240
                   ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy               241 KIVLKEKHKKACVHGGKTYSHGEVWHPAFRAFGPLPCILCTCEDGRQDCQRVTCPTEYPC 300
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Qy        361 SDLVEIYLWKLVKDEETEAQRGEVPGPRPHSQNLPLDSDQESQEARLPERGTALPTARWP 420
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Qy        421 PRRSLERLPSPDPGAEGHGQSRQSDQDITKT 451
              |||||||||||||||||||||||||||||||
Db        421 PRRSLERLPSPDPGAEGHGQSRQSDQDITKT 451
```

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (571) 272-0873. Dr. Kaufman can generally be reached Monday, Tuesday and Thursday from 8:30AM to 2:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tony Caputa, can be reached at (571) 272-0829.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Official papers filed by fax should be directed to (703) 872-9306. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.

Patent Examiner, Art Unit 1646

January 6, 2005